

Figure 1

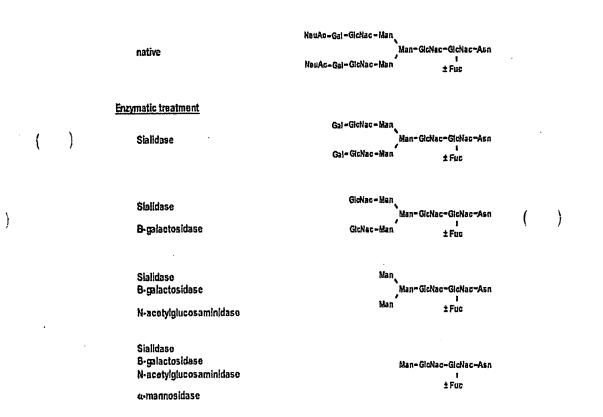


Figure 2

WO 2005/016455 PCT/BE2004/000118



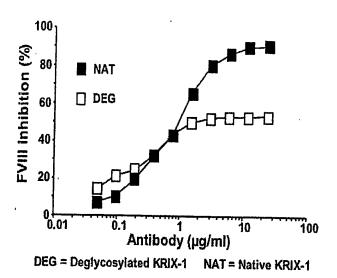


Figure 3

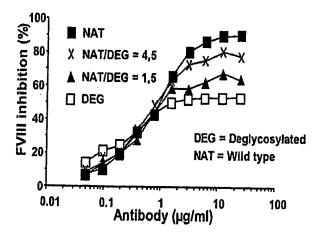
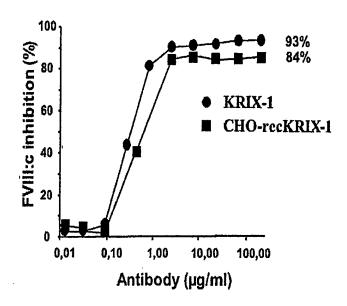


Figure 4





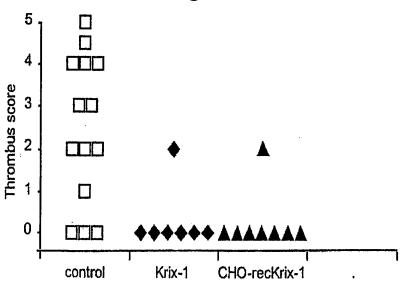


Figure 6

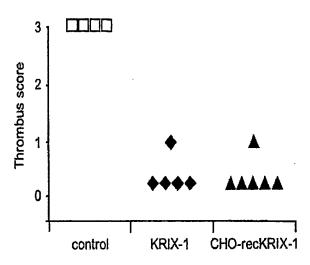


Figure 7

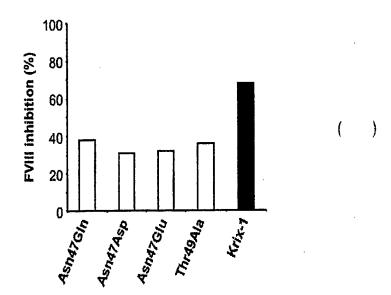


Figure 8

PCT/BE2004/000118

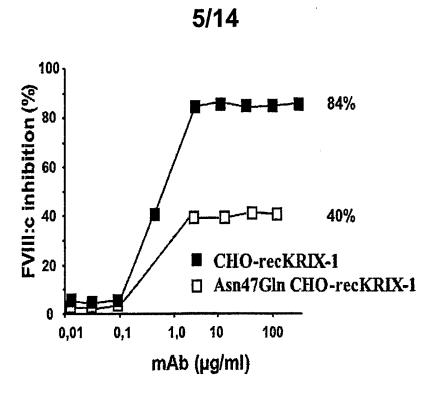


Figure 9

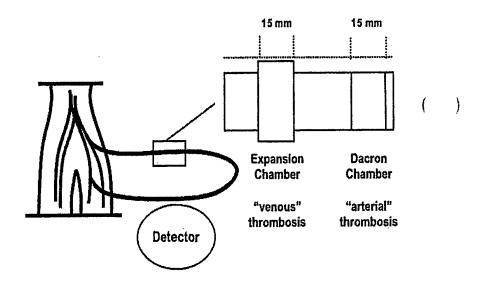
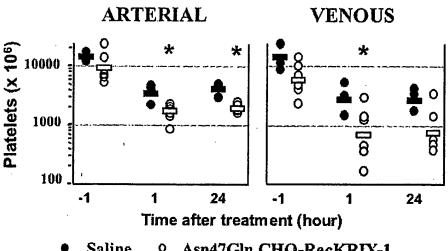


Figure 10

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- Asn47Gln CHO-RecKRIX-1 Saline
- Geometric mean p < 0.05 Mann-Whitney: Treated versus Saline *

Figure 11

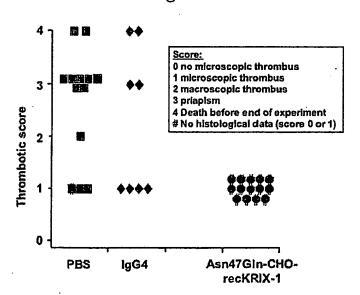
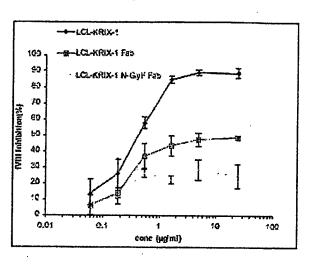
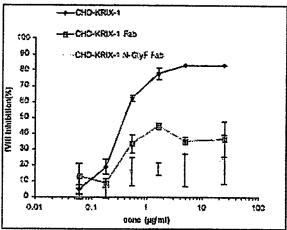


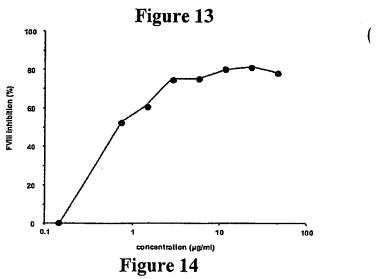
Figure 12

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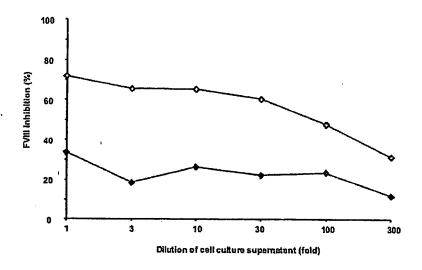


Figure 15

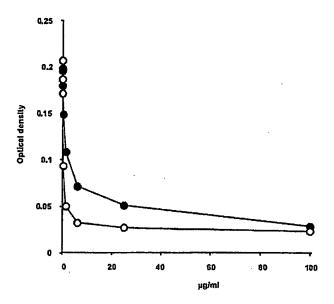


Figure 16

Krix-1 Variable heavy chain (SEQ ID NO: 1 and 2)

| М | GAC D | W | T | W | AGG R | I | L | F | L | v | GCA A | A | A | d. | G | 20 | 12 | | CAG Q |
|------------------|-----------|----------|----------|----------|----------|----------|---------|----------|----------|-------------|-------------|----------|------|----------|----------|----------|----------|----------|----------|
| 61/ GTG | 21 CAA | . CTG | | CAA | TCT | GGG | GCT | GAG | GTG | 91/ AAG | 31 AAG | | GGG | | | | | | TCC S |
| 121 TGC C | | ACC T | TCT S | G | _ | N * | F | T * | G | ¥ | TCT S | A | s | G | H | r | F | T | GCC A |
| | | | | ~ | | | | ~ | | | | | | | - CD | R1 - | | | |
| 181 | | | | | | | | | | 211 | /71 | | | | | | | | |
| Y | S | GTG V | H | TGG W | gtg V | CGA R | CAG | GCC A | CCT P | GGA G | CAA | GGG G | CTT | GAG E | TGG W | ATG M | GGA G | AGG R | ATC I |
| | | | | | | | _ | | _ | | ~ | • | _ | ~ | ••• | | G | | |
| 241 | /81 | | | | | | | | | 271, | /91 | | | | | | | | |
| AAC | CCT | AAC | AGT | GGT | GCC | ACA | GAC | TAT | GCA | CAT | AAA | TTT | CAG | GGC | AGG | GTC | ACC | ATG | TCC |
| | P | N | .s | G | A | | D 82 | | | H | K | F | Q | G > | R | V | T | M | s |
| | /101 | | | | ٠. | | | | | | | | | | | | | | |
| | | ACG | TCC | ATC | AGC | ACA | GCC | TAC | ATG | 331/ GAA | '111 CTG | AGC | AGG | ርሞር | ACA | ucu. | CAC | CNC | 300 |
| R | D | T | s | I | S | T | A | Y | M | E | L | | | L | T | | | | T |
| 361, | | | | | | | | | | 391/ | 131 | | | | | | | | |
| GCC | ATG | TAT | TAC | TGT | GCG | AGA | GCC | GAC | AAC | TAT | TTC | GAT | | | ACT | GGC | TAT | ACT | TCT |
| A | M | Y | ¥ | С | A | | | | | Y | | D | | | T | G ~ | ивз Д | T | S |
| 421/ | 44 | | | | | | | | | | | | | | | C | DRO | | |
| | | TTT | GAC | TAC | TGG · | GGC | CGG | GGA | ACC | 451/ CTG | 151 GTC | »CC | GTIC | mcc | mcs. | 000 | maa | | |
| п | I | E. | ט | Y | W | G | R | G | T | L | V | T | | | | | | | aag K |
| | | | | > | | | | | | | | | | | | | | | |
| 481/ GGC G | CCA | | | TTC F | С | | | | | | | | | | • | | | | |

Figure 17

WO 2005/016455 PCT/BE2004/000118

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Krix-1 Variable light chain (SEQ ID NO: 3 and 4)

```
ATG GAA ACC CCA GCT CAG CTT CTC TTC CTC CTG CTA CTC TGG CTC CCA GAT ACC ACC GGA
METPAQLLFLLLWLPDTŢG
<---->
                        91/31
GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA GCC ACC
EIVLTQSPGTLSLSPGERAT
                        151/51
CTC TCC TGC AGG GCC AGT CAG AGT GTT GCC AGC GCC TAC TTA GCC TGG TAC CAG CAA AAA
LSCRASQSVASAYLAWYQQK
       <---->
                        211/71
CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGT AGG GCC ACC GAC ATC CCA
P G Q A P R L L I Y G A S S R A T D I P
                        <---->
                        271/91
CAC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT CTC ACC ATC AGC AGA CTG GAG
HRFSGSGSGT
                       D
                          FTLTISRLE
                        331/111
CCT GAA GAT TIT GCA GTG TAC TAC TGT CAG CAA TAT GGT ACC TCA GCC TTA CTC ACT TTC
361/121
                        391/131
GGC GGA GGG ACC AAG GTG GAG ATC AAA CGA ACT GTG GCT GCA CCA TCT GTC TTC ATC TTC
G G G T K V E I K R T V A A P S V F I F
421/141
CCG CCA TCT
PPS
```

Figure 17 (continued)

}

scFvLE2E9VLVH Q(His) (SEQ ID 25 and 26)

| SCI | TVL. | C2C | 9 V L | V IT | ω(ΠI | S) (| 2EC | עו א | 25 a | na z | 26) | | | | | | | | |
|------------------|------------------|----------|----------|----------|----------|----------|----------|----------|---------------|------------------|-----------------|------------------|----------|------------------|----------|----------|----------|-----|-----------------|
| M | gaa E | T | P | A | Q | L | L | F | L | L | cta L | L | W | L | P | D | T | da. | : gga G > |
| 61/ gaa E | 21 att I | gtg V | ttg L | acg T | cag Q | tet s | cca | gge | : acc | 91/ ctg | 31 tct | : ttg | tet s | cca P | . ggg | gaa E | aga R | gec | acc T |
| 121, ctc L | /41 tcc S | tga C | agg R | gcc A | agt S | cag Q | agt S | gtt V | gee | 151 agc S | /51 gcc A | tac Y | tta L | gcc A | tgg W | tac Y | cag | caa | aaa K |
| P | ggc G | Q | A | P | R | L | L | I | tat Y | G | gca A | S | S | R | Α | T | ח | T | cca P |
| 241, cac H | /81 agg R | tta | agt S | gge | agt | ggg G | tct s | g 333 | | 271, gac D | /91 ttc F | act T | ctc L | acc T | atc I | agc S | aga R | cta | gag E |
| cat P \ | E | gat D | F | A | V | Y | tac Y | tgt C | cag Q | caa Q | tat Y | ggt G | T | S | A | L | L | T ' | ttc F |
| G | gga G | G | T | K | v | E | I | K | oga R > | ggt G | G | ggc G | G | S | G | G | G | æ | tct s |
| 421/ ggc G | '141 ggt G | ggc G | gga G | tog S | cag | gta V | cag Q | ctg L | gtg V | 451/ cag | '151 tot | aaa | act | gag | äta | aao | ааσ | cat | aaa |
| 481/ gcc A | tca | gtg V | aag K | V | S | C | K | T | tet s | G | tac Y | caa Q | tte F | acc T | ggc G | | | | tct s |
| 541/ gga G | cat | atc I | tte F | acc | | tac | | gtg | cac | 571/ tgg | 191 gtg | ln47 cga R | cag | hr49 gcc A | cct | gga G | caa Q | | ctt |

Figure 18

| gag E | W | atg M | G | R | I | N | P | N | S | ggt G | A | aca T | D | Y | gca A | Ħ | ĸ | TP | Λ - |
|------------------|------------------|----------|----------|----------|----------|----------|----------|----------|----------|------------------|------------------|----------|----------|----------|----------|----------|----------|----------|----------|
| | | | ~~- | | | | | | | ' | VHDJ. | н | | | | | | | |
| ggc G | ĸ | V | T | atg M | S | R | D | T | s | atc I | S | aca T | A | Y | atg M | gaa E | ctg L | agc S | agg R |
| 721, ctg | '241 aca T | tet S | gac D | gac | aça T | gcc A | atg M | tat Y | tac Y | 751, tgt C | /251 gcg A | aga R | gcc A | gac | aac N | tat Y | ttc F | gat D | att I |
| 781/ gtg V | '261 act | ggc | tat | act | tet | cat | tac | ttt | gac | 811, | '271 taa | aac: | caa | gga G | acc T | ctg L | | | gtc V |
| 841/ tcc s | tca S | H | H | H | H | H | H | | | | | | • • • • | | | | | | |

Figure 18 (continued)

RHD5 heavy chain variable region (SEQ ID NO: 29 and 30)

| 1/1 ATG M | GAC D | TGG W | ACC T | TGG W | AGG R | TTC F | CTC L | TTI F | ' GTG | 31/ GTG V | 11 GCA A | GCA A | GCT A | GCA A | GGT G | GTC V | CAG Q | TCC S | CAG Q |
|-----------------|----------|----------|----------|----------|----------|----------|----------|----------|--------|-----------------|----------------|----------|----------|----------|----------|----------|----------|----------|----------|
| < | | | | | | | | Lead | er n | enti | - ah | | | | | | | | |
| OT/ | 21 | | | | | | | | | 91/ | 31 | | | | | | | | |
| GTG | CAG | CTG | GTG | CAG | TCT | GGG | GCT | GAG | GTG | AAG | AAG | ccc | GGG | TCG | TCG | GTG | ATG | GTC | TCC |
| V | Ō. | L | V | Q | s | G | A | E | V | K | K | P | G | s | S | v | M | V | s |
| 121 | /41 | | | | | | | | | 151, | /54 | | | | | | | | |
| | | GCT | TCT | GGA | GGC | ACC | TTC | AGC | AGC | TOI, | GGT JOI | ልጥሮ | AGC | TCC | CITIC | CCN | CNC | 000 | |
| С | ĸ | A | S | G | G | T | F' | S | S | F | G | I | S | W | A C | R | Q | A | P |
| | | | | ,<· | | | | c | DR1 · | | | | > | | • | | - | | • |
| 181 | /61 | | | | | | | | | | | | | | | | | | |
| | | GGG | CTT | GAG | ጥርር | CTC | GGA | ccc | N TO C | 211, | /71 | 3.000 | mmm | | | | | | |
| G | Q | G | L. | E | W | v | G | G | I | I | P | I | F | GGT | ACA T | GCA A | AAC N | ACC | GCA A |
| | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | |
| 241/ | | mme | CAC | 2200 | 202 | ame. | | | | 271/ | /91 | | | | | | | | |
| R | N | F | CAG Q | N | R | QTC | T | ATT I | ACC | | | GAA E | TTC F | ACG T | | | | | |
| | | _ | | | | • | • | _ | • | • | ט | <u>.</u> | E | T | S | T | A | Y | I |
| | | | | | | | | | | | | | | | | | | | |
| 301/ | | | | | | | | | | 331/ | 111 | | | | | | | | |
| R | t. | AGG R | AGC S | CTG L | AGA R | TCT S | GAA E | GAT | ACG | GCC | | TAT | TAC | | | | GGT | CGA | GAT |
| | - | • | 3 | | Α. | 3 | £ | D | T | A | V | Y | Y | С | V | G | | | D |
| | | | | | | | | | | | | | | | | | < | | |
| 361/ | | | | | | | | | | 391/ | 131 | | ٠ | | | | | | |
| GCC | TAC | AGC | TTT | GAT | GGT | TTT | GAT | GTC | TGG | GGC | CAA | | | | GTC | ACC | GTC | TCT | TÇA |
| A | _ | S | F 3 | | | | | V | W | G | Q | G | T | M | V | T | V | s | s |
| | | CDI | | | | | | | | | | | | | | | | | |
| 421/ | | | | | | | | | | | | | | | | | | | |
| GCC | | | | | | | | TTC | CCC | | | | | | | | | | |
| | | | | - | | | | F | P | | | | | | | | | | |
| < | | | -con | stan | t re | gion | | | | | | | | | | | | | |

Figure 19

WO 2005/016455 PCT/BE2004/000118

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RHD5 Light Chain Variable Region (SEQ ID N0: 31 And 32)

| 1/1 | | | | | | | | | | 31/ | | | | | | | | | |
|------|-----|-----|------|------|------|------|------------|------|------|------|------|------|------|-----|------|-----|-----|------|------|
| ATG | GCA | TGG | ATC | CCT | CTC | TTC | CTC | GGC | GTC | CTT | GTT | TAC | TGC | ACA | GGA | TCC | GTG | GCC | TCC |
| M | A | W | I | P | L | F | L | G | v | T. | v | Y | _ | T | C | | 7.7 | A | S |
| < | | | -i | | | | : | Lead | er p | epti | de - | | | | | | | | > |
| | | | | | | | | | | | | | | | | | | | • |
| 61/2 | | | | | | | | | | 91/ | 31 | | | | | | | | |
| TCT | GGG | CTG | ACT | CAG | CCA | CAC | TCA | GTG | TCC | GTG | TCC | CCA | GGA | CAG | ACA | GCC | AAC | ATC | ACC |
| S | G | L | T | Q | ₽ | H | S | V | S | V | S | P | G | Q | T | A | N | I | T |
| | | | | | | | | | | | | | | | | | * | | * |
| 121/ | | | | | | | | | | 151, | | | | | | | | | |
| TGC | TCT | AGA | GAT | AAG | TTG | ggt | CAT | AAA | TTT | | | | | CAA | CAG | AAG | CCA | GGC | CAG |
| С | S | R | D | K | L | G | H | K | F | | | W | ¥ | Q | Q | K | P | G | Q |
| | < | | | | (| CDR1 | | | | | > | | | | | | | | |
| 101 | | | | | • | | | | | | | | | | | | | | |
| 181/ | | COM | omm. | omo. | 3 ma | | | | | 211, | /71 | | | | | | | | |
| S | P | A | L | L | ATC | TAT | CAA | GAC | AGC | AAG | | | | | | | | | |
| 3 | F | A | ь | T | I | Y | _ | | | | | Þ | - | G | I | P | E | R | F |
| | | | | | | | \ - | | (| JDR2 | | | > | | | | | | |
| 241/ | 81 | | | | | - | | | | 271 | /01 | | | | | | | | |
| | | TCC | AAC | тст | GGG | | | | | | | A MC | 200 | ccc | 3.00 | 010 | | 3 ma | ~~~ |
| s | G | S | N | s | G | N | T | A | T | L | | I | | G | T | | | | |
| • | _ | - | •• | • | _ | •1 | • | • | • | | _ | _ | 3 | G | T | Q | A | M | D |
| 301/ | 101 | | | | | | | | | 331, | /111 | | | | | | | | |
| GAG | GCT | GAC | TAT | TAC | TGT | CAG | GCG | TGG | GAC | | | ACT | GCC | GTA | ጥጥር | ccc | CCA | ccc | ACC. |
| E | A | D | Y | Y | С | Q | | | | N | T | | | v | F | G | G | G | T |
| | | | | | < | | | | | | | _ | | - | _ | • | • | G | • |
| | | | | | | | | | | * | | * | | | • | | | | |
| | | | | | | | | | | | | | | | | | | | |
| 361/ | | | | | | | | | • | 391/ | 131 | | | | | | | | |
| AAG | TTG | ACA | GTC | CTA | AGT | CAG | CCC | AAG | GCT | GCC | CCC | TCG | GTC | ACT | CTG | TTC | CCG | CCC | TCC |
| K \ | L | T | V | L | s | Q | P | K | A | A | P | | | | | F | P | P | s |
| } | | | | | < | | | | | | onst | ant | regi | on | | | | | - |

Figure 19 (continued)

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